November 5, 1952

Dear Luca:

As seems to happen frequently, our letters crossed in the mail, but I will hasten to reply immediately so as to restore a regular sequence.

Your modifications p. 18 and 21 are quite acceptable. I agree that the time at which segmental elimination occurs is still disputable. It is just because Lac-/Lac- homozygotes point to postmeiotic developments that I feel there is considerable leeway for other changes from the primitive zygote. Perhaps more pertinent are the occurrence of S/Mal crossovers (cf. Table 6 line 5 left; my CSH 1951 paper), still apparently hemizygous. These are rather difficult to reconcile with the prezygotic elimination. P. 423, parag. 1, fits in with this also. But I would not try to present this not entirely conclusive argument in the paper.

I am very much impressed with the elegant absorption experiment. I am reminded that Nelson, previously and now, finds a saturation level of zygotes both in Hfr x and F+ x F-, i.e., after a certain time, no more are produced. (Ca 5% max. in Hfr). I wonder if this could be related to the exhaustion of the F+. Perhaps you can do this conveniently with W-1305. That is, to test the compatibility of 58-161 cells after they have been exhausted by exposure to an excess of W-1305 cells, by then plating the mixture with W-1177 on minimal. It would also be of interest to see whether aerated 58-161 adsorbs; I have the impression instead that it can contribute the F+ agent despite its F- phenotype. You do not explicitly mention this, but I assume that the F^r type does not transmit an F agent to F-. This would have to be detected, possibly, as slowering of the fertility of exposed F- when tested with F+ (if the properties are inherent in the transducible agent).

I do have one reservation about the proposed terminology for the "virus"—I have already mentioned an objection to "virus", namely that for historical reasons this usage will be confused with lysogenic phages. The experiments certainly point to a specific agent, potentially separable from the cells, but I would like to refrain from giving it a special symbolism until it has actually been separated from the cells. ϕ itself would be an unfortunate symbol, as it is used widely for phages. I am afraid there is the possibility that too specific a set of symbols may obscure interpretations by which the F+ agent is not a unique particle (though I admit I have not been successful in formulating these). It has occurred to me that Hayes' concept of the F+ agent itself as the vehicle of recombination can be brought into formal agreement with ours if we identify the F+ agent as the cell itself, in the F+ state. This state is transducible presumably by cell-to-cell contact, which, in a certain fraction of cases may also result in the transmission of a nucleus. In Hfr, although the F+ state itself is not transmissible, perhaps every contact results in nuclear transmission. Calculations of collision efficiency are close to 1 both for the F+ transduction and the Hfr recombination; ~~for the saturation of the latte~~

Nelson is only just now getting deeply into the kinetic studies; so far, there has been an obligatory association of recombination with active growth. I am waiting to see these studies pushed a little further before continuing with the cytology, and I have nothing to report. Concerning the distribution of Hfr, I think that Delbruck-Vogt now fully understand that the cultures previously sent were degenerated. Vogt herself is no longer working on recombination. Judging from past experience, I would say that one cannot reserve any "special uses of a strain" after distributing it, unless there is an active collaboration. I should say that you would be fully justified in reserving the strain itself until the studies now in progress have been completed. Frankly, I think that its distribution at the present time would lead to confused talk rather than any further progress, and I hope that any immediate embarrassment will not be so severe as to lead to a change in policy. [We have tried the alternative of discussing the fields of immediate interest, and it has not worked out well at all.] Since I am urging this on you, I am prepared to share the responsibility for it.

You mention that the filtration experiments may be in question owing to the limited contagiousness of the F+ agent. My experiments along these lines have involved very considerable proliferation, which should have allowed the "generalization" of the F+, if it developed, but perhaps this should be reviewed in reconstruction experiments.

As soon as the kinetic studies reach any definite conclusion, I will relay them to you. They are, of course, rather laborious. So far, we have been mainly concerned with Hfr x F- under various conditions, and have only just begun a consideration of techniques for studying F+ transmission. In view of your present successes, perhaps the emphasis on this should be shifted to Milan? If any technical advances develop, we will let you know at once, of course.

Sincerely,

Joshua Lederberg